Cost-benefit analysis of Helicobacter pylori screening

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The study compared two intervention strategies for the management of Helicobacter pylori (Hp). Strategy 1 was population-based Hp screening with subsequent treatment for all positive screened individuals. Strategy 2 was no screening, with the testing and treatment of Hp only if associated clinical symptoms were documented. Screening was performed using an enzyme immunoassay to investigate serum immunoglobulin (Ig)G and IgA antibodies to Hp. Lower limits of raised titres were 700 for IgG and 70 for IgA antibodies. Treatment, which was administered for 1 week, consisted of amoxycillin (1,000 mg x 2), clarithromycin (500 mg x 2) and omeprazole (20 mg x 2).

Type of intervention
Screening and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population was derived from a published study (Salomaa et al. 1998, see ‘Other Publications of Related Interest’ below for bibliographic details). It was reported that the study population comprised all individuals aged 15 to 40 years in 1996 and all individuals aged 15 to 45 years who lived in Vammala (southwest Finland). Individuals aged above 45 years were not included in the study. Altogether 5,288 individuals were included. No further inclusion or exclusion criteria were reported in the current study.

Setting
As this was a modelling study the setting was not explicitly stated. However, the setting appears to have been primary care and patients continued their everyday life in the community.

Dates to which data relate
The effectiveness data were derived from studies published between 1979 and 2003. The costs were derived from sources published in 1999 and were reported for the financial year 1998 to 1999.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of completed studies, and were augmented by authors’ assumptions.

Modelling
The authors constructed a decision analytic model (decision analytic tree) to estimate the costs and effectiveness of the two interventions. The time horizon of the model was the patients’ lifetime. The model was based on certain assumptions. For instance, third treatment failure, the possibility of re-infection after cure, and spontaneous eradication
without therapy were not accounted for in the model. In addition, as the lifetime risks of Hp-related diseases were
disease-specific, successive Hp-related diagnoses were not included in the model.

Outcomes assessed in the review
The input parameters derived from the literature for use in the model were the probability estimates for Hp screening-
related variables and Hp-related disease variables. A full breakdown of the specific probabilities was presented in the
paper.

Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Overall, 26 primary studies provided effectiveness data.

Methods of combining primary studies
Methods for combining the primary studies were not reported.

Investigation of differences between primary studies
It was not explicitly stated whether differences between the primary studies were investigated.

Results of the review
The screening participation rate was 76% (range: 61 to 90).

The prevalence of Hp antibodies indicating infection was 13% (range: 10 to 16).

The sensitivity of the screening test (serology) was 97% (range: 90 to 98) and the specificity was 93% (range: 90 to 98).

The visit rate was 87% (range: 70 to 90).

First, second and third compliance rates were 86% (range: 69 to 90), 47% and 50%, respectively.

The effectiveness of first and second treatments were 81% (range: 5 to 90) and 82%, respectively.

The lifetime probabilities of gastric cancer, duodenal ulcer (DU) and gastric ulcer (GU) in the general population were
0.004, 0.1 and 0.035, respectively.

Hp-related gastric cancer of all gastric cancers was 73%.
The lifetime probabilities of Hp-related gastric cancer, DU and GU if Hp positive were 0.022 (range: 0.005 to 0.03), 0.12 (range: 0.11 to 0.22) and 0.028 (range: 0.02 to 0.04), respectively.

The lifetime probability of diagnosed Hp-related premalignant lesions (PL) if Hp positive was 0.09 (range: 0.02 to 0.12).

The probability of operational treatment of PL was 0.11.

The proportions of DU and GU due to being Hp positive were 0.95 and 0.8, respectively.

Hp prevalence in population where DU and GU were studied was 0.8.

DU and GU diagnosed in emergency care was 0.05.

The probability of survival when GU and DU were diagnosed in emergency care was 0.92.

The probabilities of bleeding complications due to DU and GU were 0.004 and 0.002, respectively.

The lifetime probability of Hp-related functional dyspepsia if Hp positive was 0.05.

Helicotest urea breath test sensitivity was 98%.

Compliance regarding dyspepsia 91%.

**Methods used to derive estimates of effectiveness**

Some methods of effectiveness were based on authors’ assumptions.

**Estimates of effectiveness and key assumptions**

The sensitivity and specificity of re-tests were assumed to be 100%. The probability of failure of a third treatment was assumed to be 0%.

**Measure of benefits used in the economic analysis**

The measures of benefit used were the number of treated Hp infections due to screening and the number of cases (i.e. persons invited for screening with the two interventions). These were directly derived from the model.

**Direct costs**

The health service unit costs were included in the analysis. These were for the screening invitation, Hp serologic diagnostic test, general and screening general practitioner visit, first gastroenterologist visit, gastroscopy for normal and extensive biopsies, 4-week treatment using H2 antagonist, 4-week proton-pump inhibitor treatment, 4-week antacid treatment, 4-week nonsteroidal anti-inflammatory treatment, first Hp eradication, adverse effect treatment (average cost), Hp urea breath test, surgery for PL, complicated and uncomplicated gastrointestinal bleeding, intensive care unit inpatient care, and intensive care unit surveillance. The costs incurred before diagnosis were derived from a published study and augmented by expert opinion. Further costs were based on actual data derived from the Helsinki University Hospital. The costs and the quantities of resources used were reported separately. All costs were reported for the price year 1998 to 1999. As the costs were incurred during more than 2 years, discounting was appropriately carried out.

**Statistical analysis of costs**

The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
The authors converted Finnish markka (FIM) to US dollars ($) using the official exchange rate in January to September 1999 ($1.00 = FIM 5.54). All costs were reported in US dollars ($).

**Sensitivity analysis**
The authors conducted one-way sensitivity analyses to investigate the robustness of the results to variability in the data. Screening-related parameters were changed by +/-20% in spite of the probabilities of participation, visit, compliance and effectiveness of treatment rates, which were not estimated to surpass 90%. Hp-related disease probabilities were also investigated in the one-way sensitivity analyses. The ranges used were derived from the literature and were reported in full.

The unit costs of screening test, general practitioner visit, and aggregated costs of Hp-related diseases were also varied by +/-20%.

In addition, the authors conducted multivariate sensitivity analyses investigating the cost per case when patients received screening at 15, 30 and 45 years of age. The age-specific variables, which were varied simultaneously, were the participation rate, visit, compliance rate, prevalence, and all the discounted cost variables. Age-specific ranges were derived from a published study.

A second multi-way analysis was conducted to test the robustness of the results to variability in the lifetime probabilities of developing Hp-related disease (gastric cancer, PL, DU, GU, dyspepsia). The probabilities were varied simultaneously around minimum and maximum values, which were derived from the literature.

A probabilistic sensitivity was carried out, using a Monte Carlo simulation of 1,000 cases and adopting a logistic or uniform probability distribution for the ranges of 22 selected parameters.

**Estimated benefits used in the economic analysis**
The estimated benefits were not reported separately.

**Cost results**
The total intervention costs were not reported separately. However, the authors presented selected undiscounted aggregated costs (used in the decision analysis) of cost-causing events of dyspepsia, including events prior to diagnosis, immediate or delayed diagnosis, and eradication.

**Synthesis of costs and benefits**
In the screening option, the cost per case (i.e. per person invited) was $69 for screening and $43 for the no screening option.

An incremental analysis was also performed. It was reported that the incremental cost per treated Hp infection as a result of screening was $412.

The sensitivity analyses demonstrated that the incremental cost per case was highest in the group aged 15 years and lowest, resulting in cost-savings, in the group aged 45 years.

The incremental cost per case was $38 when minimum estimates of all disease probabilities were used and $15 when maximum values were used.

The probabilistic sensitivity analysis gave values for screening versus no screening as follows:
mean, $68.7 versus $43.1;
standard deviation, $4.5 versus $5.3;
minimum, $55 versus $27; and
maximum, $81 versus $63.

The results of the one-way sensitivity analyses demonstrated that the results were most sensitive to changes in the estimated probability of Hp-caused gastric cancer and gastric PL.

Authors' conclusions
Screening for Helicobacter pylori (Hp) is more favourable in the older age cohorts.

CRD COMMENTARY - Selection of comparators
The authors compared universal population-based screening for Hp in patients aged between 15 and 45 years versus no screening. You should decide whether this represents a valid technology in your own setting.

Validity of estimate of measure of effectiveness
No systematic review of the literature was undertaken. Although this is common practice with models, it does not always ensure that the best data available are used in the model. The estimates of effectiveness from individual studies were not combined as the available data appear to have been used selectively. In addition, the authors did not consider the impact of differences between the studies identified when estimating effectiveness. Some estimates of effectiveness were based on authors' assumptions, but the choice of assumptions was not explicitly justified. However, the authors carried out several sensitivity analyses relating to the efficacy estimates. These analyses improve both the internal validity and the generalisability of the study by demonstrating the robustness of the results to changes in the base-case estimates.

Validity of estimate of measure of benefit
The authors used number of cases and number of Hp infections treated on account of screening as measures of benefit in the economic analysis. The measures of benefits were derived directly from the model.

Validity of estimate of costs
The perspective adopted in the economic analysis was not explicitly stated. However, it does not appear to have been societal since the indirect costs were not included in the analysis. The unit costs were reported, as were aggregated costs corresponding to specific resources used, thus enhancing the reproducibility of the study in other settings. Resource use and costs were based on actual data and published sources, and extensive sensitivity analyses were carried out to investigate the robustness of the estimates used. The ranges used in the sensitivity analyses appear to have been appropriate. Appropriate currency conversions and discounting were carried out and the price year was reported.

Other issues
The authors compared their findings with those from other studies and generally found them to be in agreement. The issue of the generalisability of the results to other settings was not directly addressed, although the probabilistic sensitivity analysis may help. The authors do not appear to have presented their results selectively. The authors reported a number of limitations to their study. First, the impact of negative effects due to Hp treatment and the impact of curing Hp infection on reflux oesophagitis and primary adenocarcinoma of the oesophagus were not investigated. Second, owing to a lack of adequate data, some of the Hp-related outcomes were not based on robust data, thus introducing uncertainty into the results. However, extensive sensitivity analyses were carried out to investigate the robustness of the estimates used.
Implications of the study
The authors did not make explicit recommendations for changes in policy or practice. However, they called for further research to explore the negative effects of Hp treatment and extensive use of antibiotics, as well as the impact of Hp screening on quality of life. The authors also called for an economic analysis that will account for non-health care and time costs.

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Other publications of related interest

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